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The Hunterian Lectures

ON

THE RENAL FUNCTION IN ITS RELATION TO SURGERY

Delivered before the Royal College of Surgeons of England

BY

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DEC 07

Reprinted from THE LANCET, March 16 and 23, 1907

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ON

THE RENAL FUNCTION IN ITS RELATION TO SURGERY.

LECTURE I.

Delivered on March 1st, 1907.

MR. PRESIDENT AND GENTLEMEN,—A consideration of the renal function in its relation to surgery opens up a wide field for investigation and observation in surgical pathology, in diagnosis, and in treatment. To pass in review only the main features of the subject included under each division would expand these lectures beyond the necessary limits that are placed upon them. I have, therefore, selected for the subject of discussion one of these divisions—namely, the diagnosis of the renal function so far as it is related to surgery. And this subject recommends itself more naturally for the theme of a Hunterian lecture since it treats of facts which lie on the borderland between the science and the art of surgery.

In his Hunterian lectures for 1898 Mr. Henry Morris traced the origin and progress of renal surgery up to that date, and he showed how, commencing with the pioneer nephrectomy of Simon in 1869, renal surgery had progressed step by step to nephrotomy (Annandale, 1869; Spencer Wells and Bryant, 1870), nephrolithotomy (Morris, 1880), nephropexy (Hahn, 1881), and partial nephrectomy (Czerny, 1887). The problem which was solved by nephrectomy was whether one healthy kidney could carry on the entire renal function after the shock of the operation of nephrectomy. Hæmorrhage from the healthy kidney substance was the obstacle that was swept aside by Morris's nephrolithotomy and, in addition, the proof was obtained that the incision of a healthy kidney would heal without permanent damage to the organ. In the kidney, as in other organs, operative attack laid bare the limited means of diagnosis at the command of the surgeon and stimulated further efforts in the direction of greater accuracy. What became evident was this: that with these fundamental facts well established, with the great advance provided by the introduction of antiseptics, and with every

precaution against surgical shock, there still remained a mortality in the operative surgery of kidney disease against which provision had not been made. This mortality resulted from a failure of the renal function. It is brought about in several ways: the disease may be bilateral and so far advanced that the renal function is only just sufficient for the wants of the individual. An operation of any kind may be sufficient to overbalance the impaired renal function and lead to suppression of urine. The frequency with which this may occur in operations which do not concern the urinary system is difficult to estimate, but it is probably not great, for the presence of advanced renal disease would be looked upon as a sufficient contra-indication to any but operations of urgency. I shall not, therefore, pursue this subject further. When the operation concerns some part of the urinary tract, however, this mortality at once becomes a prominent factor and a consideration of the adequacy or the reverse of the renal function is likely to arise. Thus, in operations upon the lower urinary tract, suppression of urine takes a high place in the mortality figures. Finally, in operations upon the kidney, the question as to the renal efficiency becomes a matter of importance.

In my second lecture I shall consider the question of the second kidney in nephrectomy, and it need only be remarked here that such a catastrophe as the removal of a kidney when the second kidney is destroyed by disease, or when only one kidney has developed, demonstrates the need for a complete estimation of the renal function. But apart from the removal of the kidney there are cases of bilateral disease in which a conservative operation upon one organ is sufficient to upset the balance of renal secretion and cause fatal suppression of urine. An attempt to estimate the renal function in these cases has for its object not only the demonstration of a lowered renal function, for that may be already obvious, but the decision, if this be possible, as to whether the function is lowered to such a degree that operation will almost certainly prove fatal. I shall therefore consider the subject of the estimation of the renal function, so far as it concerns surgery, under two main divisions: (1) the estimation of the total renal function; and (2) the estimation of the function of one kidney.

1. The Estimation of the Total Renal Function.

Until a comparatively recent date the surgeon has been content to rely upon the symptoms and local signs of renal disease and the examination of the urine in order to judge of the activity or the reverse of the kidneys. I shall not dwell upon these. The kidneys may be exposed by operation and examined with a view to estimate the renal function. Palpation of the kidneys by the abdominal route has fallen into disuse from its unreliability. The exposure and examina-

tion of the kidneys by lumbar incision where the stability of the renal function is in doubt involve a risk which the surgeon may wish to avoid. And, moreover, it is not always easy to judge of the functional power of a kidney so exposed. In a case of suppression of urine following an operation upon a stricture I cut upon the kidney and stripped the capsule in the hope of relieving the renal tension that is supposed to exist in these cases. The kidney was flabby, and except for venous congestion did not differ in appearance, size, or consistence from a fully functional kidney. It is possible that some method may be developed by which fully functional kidney tissue can be recognised.

In a case of exploration of the kidney where I had used the methylene blue test for the purposes of diagnosis, and where the blue colour of the urine was still strongly marked, I hoped to find on incising the kidney that the exposure to air would produce the blue colour observed in animals that are passing methylene blue, and that I should thus be able to recognise the extent of the fibrous changes in the renal substance by the variations of staining. I was disappointed, however, for no change in colour was observed. Nor did the use of peroxide of hydrogen as an antiseptic during the operation bring out the colour.

I shall at once pass to the consideration of certain methods of estimating the renal function which have been introduced at a comparatively recent date.

Although it cannot be said that the physiology of the renal function is fully known, certain phenomena are recognised as being either a part of the function or inseparably connected with it. 1. The kidneys separate from the blood a fluid of different molecular composition—namely, the urine. The osmotic pressure of the urine is greater than that of the blood and the work performed by the kidney may be measured by estimating the osmotic pressures of these two fluids. This is conveniently done by investigating the freezing point of these fluids (cryoscopy). 2. The kidneys exercise a selective power by which certain substances are removed from the blood. Thus certain of the constituents of the urine do not appear in other secretions of the body, although they circulate in the blood. In similar manner certain foreign substances introduced into the blood are eliminated by the kidneys. Thus iodide of potassium, salicylate of sodium, and other drugs are passed out in the urine, and certain dyes, such as methylene blue, fuchsin, and rosaniline, may be recognised in the urine by the changes in colour which they produce. The kidneys are also said to have the power of removing certain toxic bodies from the circulation, the accumulation of which would produce the syndrome of uræmia. 3. It is further recognised that the kidneys have a synthetic action in regard to at least one substance (hippuric acid) which exists in small quantities in the urine and they are thus brought into line with glandular organs. It is known that the administration of phloridzin is

followed by the temporary appearance of glucose in the urine and that the glucose is produced by the vital action of the kidney. 4. Finally, a controlling function over nitrogenous metabolism by means of an internal secretion has been suggested by certain experiments. The methods of estimating the renal activity which follow are dependent upon the examination of some of these functions.

1. *The Kidney as a Filter: (a) Cryoscopy.*

Dresser[1] has shown that the osmotic pressure of the urine is considerably in excess of that of the blood. If the kidneys are diseased their power of bringing about a change in the osmotic tension of the fluid passing through is reduced and the freezing point of the urine is raised. The credit of introducing this method into clinical medicine belongs to Koranyi of Budapest.[2] Koranyi has advanced a theory of renal secretion upon which several tests are based. This observer suggests that a solution of sodium chloride filters from the blood into the renal tubules at the glomeruli. As this solution passes down the tubules it is concentrated by the absorption of water, and an interchange of molecules between the solution and the blood takes place through the renal cells. Each molecule of sodium chloride which is passed from the urine into the blood is replaced by a molecule of a different nature, such as urea, uric acid, &c., derived from the blood.

The following methods are based upon the estimation of the molecular content of the urine and the blood by measurement of the freezing point:—

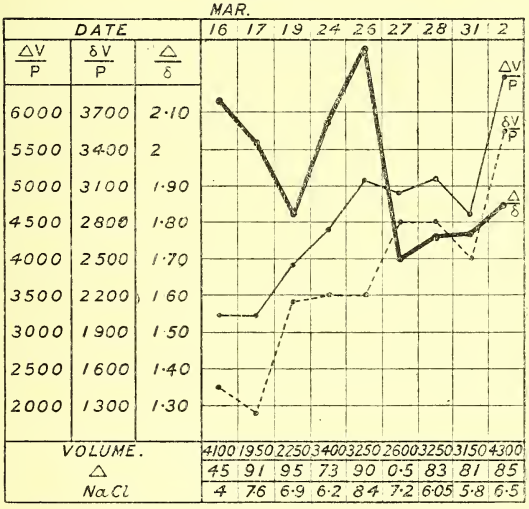
Cryoscopy of the urine.—The freezing point of the urine (point Δ U) represents the molecular concentration of the fluid without reference to the nature of the dissolved substances. In the healthy state it is liable to considerable variations. Koranyi places it between $-1\cdot30°$ and $-2\cdot30°$ C. Copious libations may raise it to $-1°$ C. and profuse sweating may lower it to $-2\cdot30°$ or under. In nervous polyuria it may rise to $-0\cdot17°$ C. In a large number of urines there is a precipitation of urates at the freezing point and this materially affects the calculation. The quantity of molecules thus thrown out of solution is a variable factor, so that no correction can be made which will apply to all urines. The mixing of alkaline and acid urines also induces changes in the freezing point. Apart from these fallacies, however, the variations in the freezing point of the urine are so considerable in the healthy individual that no trustworthy observations can be made by this method.

[1] Archiv für Experimentale Pathologie und Pharmakologie, 1892, Band xxix., S. 307.

[2] Zeitschrift für Klinische Medicin, 1897, vol. xxxiii., Nos. 1-2; Berliner Klinische Wochenschrift, 1899.

According to Koranyi's theory the number of molecules of sodium chloride in the urine will depend upon the interchange of urea, &c., which has taken place in the renal tubules. By dividing the figures of the freezing point by the sodium chloride content per 100 cubic centimetres of urine, Koranyi hopes to estimate the work of the renal epithelium. The figures work out at 1·7, or in a series of cases at 2 or over. The more rapidly the sodium chloride solution is hurried past the renal epithelium the less will be the interchange of molecules, so that the product of this formula is smaller.

FIG. 1.



Period of temporary renal inefficiency in chronic nephritis (Claude and Balthazard).

The volume of urine thus comes to be an important factor. Claude and Balthazard[3] correct Koranyi's formula for both the volume and the total body weight and term the product the "total molecular diuresis." By calculation they ascertain from this the "diuresis of elaborated molecules," and after correcting this again for volume and weight they obtain the "sum of the molecular interchange" by the renal epithelium by dividing the former by the latter product. The accompanying chart (Fig. 1) shows in a graphic form a

[3] Journal de Physiologie et de Pathologie Générale, 1903, 97.

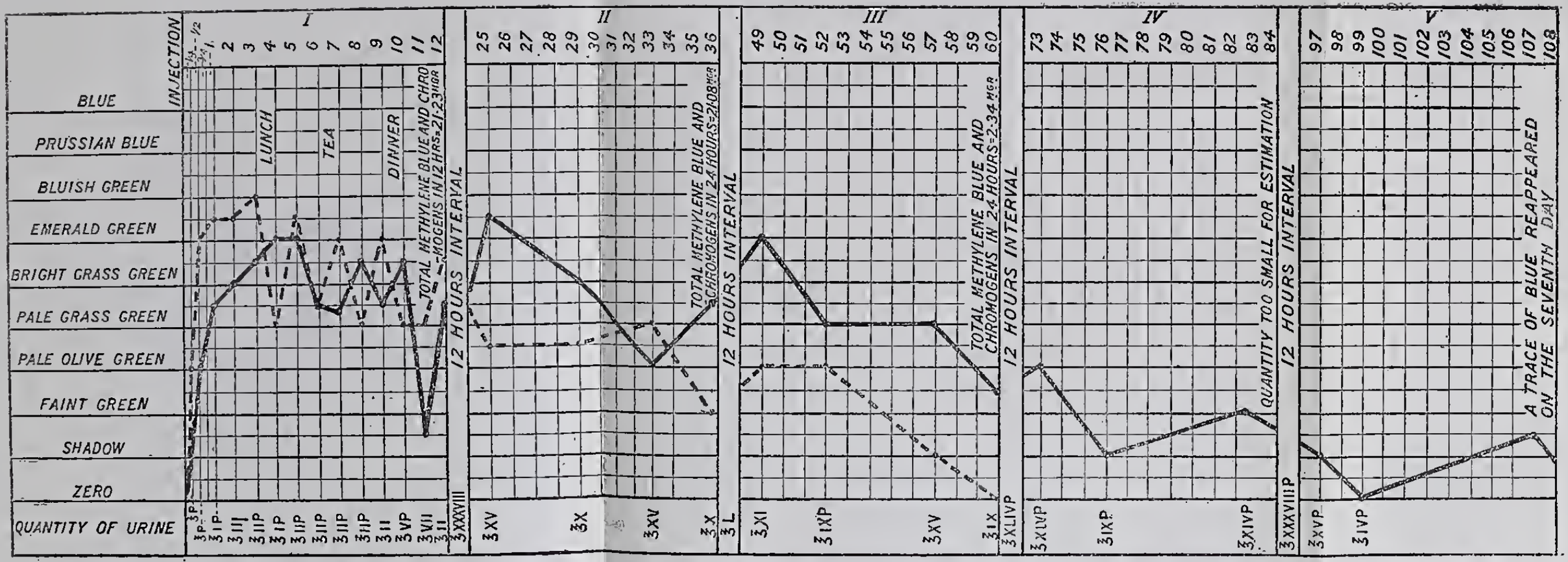
period of renal inefficiency in a case of chronic nephritis. The elabarate calculation thus entailed depends upon several factors each of which is liable to fallacy. It is known that there is a retention of chlorides in renal diseases and Claude and Mauté [4] make use of this fact to observe the result of a measured administration of chlorides compared with cryoscopy.

Cryoscopy of the blood.—The freezing point of the blood is remarkably constant at $-0\cdot56°$ C., and the point Δ of the serum is practically the same as that of the blood. According to Koranyi, where one kidney is inefficient no change is found in the freezing point, but where the function of both kidneys is impaired the freezing point of the blood is lowered. A freezing point of $-0\cdot57°$ to $-0\cdot58°$ indicates a reduction in the total renal function. This margin of reduction is, however, too small and a point Δ of $-0\cdot59°$ or $-0\cdot60°$ should be shown before bilateral disease is diagnosed. Kümmel [5] looks upon a freezing point of $-0\cdot60°$ as a contra-indication to nephrectomy, and he believes further that when the molecular concentration is normal there is no interference with the total renal function. In 16 cases of bilateral renal disease this observer found the freezing point of the blood was from $-0\cdot60°$ to $-0\cdot65°$, and in one case it was $-0\cdot71°$. In 11 cases in which nephrectomy was performed a freezing point before the operation of $-0\cdot56°$ was taken as a proof of a healthy second kidney. After the operation the remaining organ in all the cases continued to secrete a sufficient quantity of healthy urine, and the freezing point of the bloood remained at $-0\cdot56°$. In one case the freezing point before operation was $-0\cdot59°$ and after the operation $-0\cdot57°$. It is undoubted, however, that a lowered point Δ of the blood to $-0\cdot60°$ may be found apart from lesions of the kidneys. In my own cases the method has proved trustworthy but the number of cases in which I have used it is small. In cases where the point was depressed I was able by other means, such as the methylene blue test or phloridzin glycosuria, to confirm the inadequacy of the renal function or the symptoms were such as to leave no doubt upon the subject. In a case of enlarged prostate I disregarded a freezing point of the blood of $-0\cdot66°$ C. as the symptoms of renal inefficiency were insignificant. The patient succumbed to suppression of urine after the operation. In another case where obstructive anuria was in progress the point Δ of the blood was $-0\cdot71°$ C.

Comparative cryoscopy of the urine and blood.—In the comparative cryoscopy of the urine and blood (Bernard [6]) the

[4] Société Médicale des Hôpitaux, 2 Mai, 1903.
[5] Beiträge zur Klinische Chirurgie, 1903, 37.
[6] Thèse de Paris, 1900.

FIG. 2.



Elimination of methylene blue in a healthy individual. The elimination was prolonged as traces beyond the normal duration. Blue shown by dark continuous line, chromogen by dotted line. The chart shows the total daily elimination of blue and chromogen in milligrammes and the total quantity of urine in ounces.

ideal method for the estimation of the work done by the kidneys would appear to be provided. The freezing point of normal urine is from $-1\cdot5°$ to $-2°$ and that of blood serum $-0\cdot56°$. The quotient of these will be $2\cdot5$ to $3\cdot5$ and when this figure diminishes we may conclude that there is a diminution in the permeability of the kidney. These figures are, however, affected in the same way as those of the urine alone. The wide range of variation of the freezing point of the urine in health will disturb the figures considerably. Bernard has endeavoured to correct this fallacy by introducing the volume of the urine in cubic centimetres into the calculation. The figures thus obtained will vary in normal individuals from 3000 to 5000. If we test this method on two types of cases—namely, a case of polyuria from interstitial changes in the kidneys the result of an enlarged prostate and a case of obstructive oliguria almost amounting to anuria—it will be found that the products of these formulæ successfully show the impaired function when oliguria is present, but fail to demonstrate the condition where polyuria is present.

(*b*) *Method of Wright and Kilner.*

Wright and Kilner[7] have taken advantage of the fact that complete destruction of the red blood corpuscles (hæmolysis) occurs at a certain point of dilution of the blood serum and under similar conditions in a suspension of blood corpuscles in urine, and use this as an indication of the dilution of these fluids. The result is expressed in the number of dilutions required to bring about the hæmolysis.

(*c*) *Electrical Resistance of the Urine.*

Aqueous solutions offer a variable resistance to the passage of an electrical current according to their composition, and Bordier of Lyons[8] has applied this method to the examination of the urine. The urine owes its conductivity almost entirely to its mineral constituents and not at all to its organic contents. According to Dr. Dawson Turner[9] the results of this method in renal disease correspond very closely to those of cryoscopy.

2. *The Elimination of Certain Substances in the Urine.*

It has long been recognised that the elimination of certain substances in the urine is hindered by disease of the kidneys. This subject has received the attention of Hahn, Rayer,

[7] The Lancet, April 2nd, 1904, p. 921.
[8] Quoted, Debove, Achard et Castaigne: Maladies des Reins, 1906.
[9] Practical Medical Electricity, third edition, 1902.

Roberts, Duckworth, and others. Achard and Castaigne[10] in 1897 introduced methylene blue as a drug on which observations might readily be made. Fuchsin was used with a similar object by Bouchard and Lepine[11] studied the elimination of rosaniline. Observations have also been made upon the elimination of iodide of potassium and the subject has been reviewed by Lafaye.[12] while Sée,[13] Chopin,[14] and others have studied the elimination of salicylate of sodium.

(*a*) *The Methylene Blue Test.*

If methylene blue be administered in the form of pill or injected into the muscles the urine will, after a time, assume a blue or green colour. Intramuscular injection is preferable on account of the greater accuracy. Methylene blue is absorbed into the blood from the point of injection as a colourless derivative and this reduction takes place only by the action of living tissues. Microscopical examination of the blood shows no colouration of the plasma or of the white corpuscles and the spectroscope shows no change. Nor can this leuco-derivative be detected in the blood by the means by which it is demonstrated in the urine. The colourless derivative or chromogen is transformed into methylene blue by the liver and the kidneys and is excreted in the bile and the urine. The blue in the bile is apparently re-absorbed in the intestine. Methylene blue is eliminated in the urine in two forms, partly as methylene blue and partly as a colourless derivative or chromogen. The latter is transformed into methylene blue by boiling with acetic acid. About 50 per cent. of the total quantity of methylene blue injected is eliminated by the kidneys in the first 24 hours, but only part of the total methylene blue is passed by the urine. The elimination of methylene blue in a healthy individual is shown in Fig. 2.

In studying the elimination of methylene blue there are several points which claim attention: (1) the commencement of elimination; (2) the duration; (3) the quantity of colouring material eliminated as blue and as chromogen; and (4) variations in the course of elimination.

1. *The commencement of the elimination.*—Chromogen appears in the urine 15 minutes after the injection and the blue usually commences in half an hour. This relation of chromogen and methylene blue was the rule in my cases in health and disease. In pathological conditions of the kidneys the elimination of blue is delayed and may occur after one or three or even several hours. Occasionally the blue does not

[10] Bulletins et Mémoires de la Société Médicale des Hôpitaux, 30 Avril, 1897, p. 637.

[11] Lyon Médicale, p. 251, 1898.

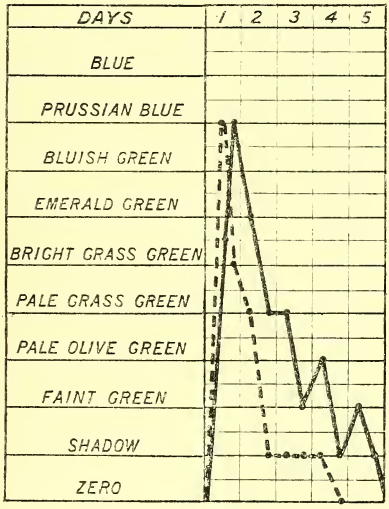
[12] L'Elimination Urinaire de l'Iode, Paris, 1893.

[13] Bulletin de l'Académie de Médecine, 1877, p. 717.

[14] Thèse de Paris, 1889.

appear at all. The period of delay is to some extent a measure of the severity of the renal lesion, but cases are on record where a considerable delay was occasioned by renal lesions of an insignificant character. When the blue is delayed the chromogen is usually delayed also. Thus in two cases of malignant disease of the prostate without symptoms of renal disease methylene blue elimination was delayed three and four and a half hours and chromogen elimination 53 minutes and four and a half hours respectively. But, on the other hand, a normal commencement of chromogen may be observed when the blue is

FIG. 3.



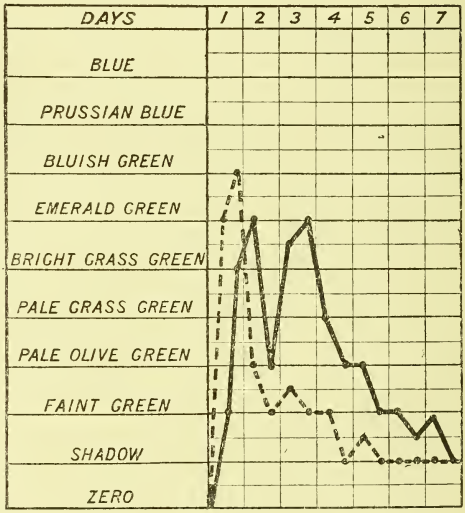
Elimination in healthy subject prolonged to fifth day. Blue shown by continuous line, chromogen by dotted line.

delayed. In a case of "fibrous prostate" methylene blue appeared in two and a half hours and chromogen in 15 minutes, and in a case of renal pain where the kidney had been explored three years previously the blue was delayed three and three-quarter hours and the chromogen appeared in 15 minutes. Where the blue does not appear in the urine at all the chromogen may appear late. In a case of pyonephrosis the chromogen appeared alone in one and a quarter hours and in a patient suffering from advanced bilateral pyelonephritis the chromogen appeared alone in one hour. An early onset (under 30 minutes) of

elimination of blue has been observed by Bard[15] in epithelial nephritis. This early appearance of blue has also been noted in some cases of hypertrophy of one kidney (Albarran).

2. *Duration of elimination.*—In a healthy subject the whole excretion of blue is said to be completed in from 35 to 60 hours. My own observations seem to show that this period is too short. After the first wave of elimination had passed traces were observed in the urine during the fourth, fifth, and even on the sixth days in some healthy individuals.

FIG. 4.



Elimination in healthy subject prolonged to seventh day. Blue shown by continuous line, chromogen by dotted line.

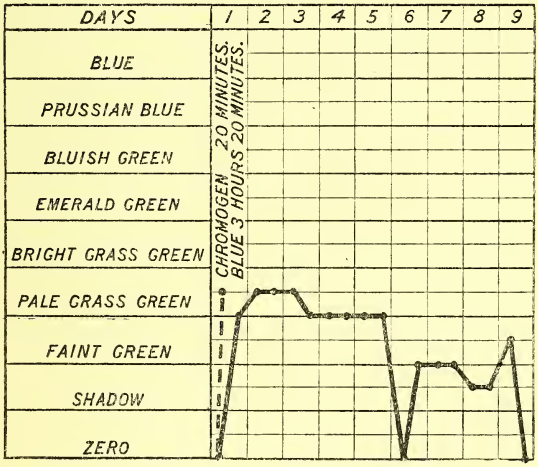
(Figs. 3 and 4.) In pathological conditions of the kidney the excretion may take place within those limits, but the duration is usually prolonged, more rarely it is shortened.

Shortened elimination.—An excessive quantity of methylene blue may be rapidly passed. This occurs, according to Bard, in parenchymatous nephritis. The shortened elimination may coincide with a considerable reduction in the quantity of blue eliminated. In these cases there is extensive

[15] Gazette Hebdomadaire, 27th Mai, 1907, p. 494.

disease of the kidneys. According to Achard and Castaigne [16] this short elimination occurs at the period when the blue is present in the blood in greatest quantity, and when the quantity of blue in the blood fails the kidney does not allow it to pass through. This does not, however, explain cases where the blue fails entirely to appear in the urine or only shows as a faint trace, yet the chromogens are excreted in fair quantity during a varying period. It appears to me that the difficulty lies in the transformation of the chromogen of the blood into methylene blue and that the diseased kidneys lack this power.

FIG. 5.



Enlarged prostate, interstitial nephritis. Delayed, prolonged, and diminished elimination of blue with single intermission on sixth day.

Prolonged elimination.—With a reduced quantity of renal tissue in disease of the kidneys the elimination of blue is prolonged. This is observed to a marked degree in chronic interstitial nephritis where traces of blue may persist for from six to ten days and more, rarely so long as 15 days. Prolonged elimination is also observed in surgical disorders of the kidneys. I have observed the elimination of blue during a period of eight days and 17 hours in a man, aged 67 years, who suffered from enlarged prostate and interstitial nephritis (Fig. 5). Faint traces are sometimes passed for

[16] Des Fonctions Rénales, 1900.

several days in individuals whose kidneys are healthy. In a healthy subject I was able to detect traces of blue on the sixth and seventh days after injection. There had, however, been intervals of clear urine. In a slight degree of renal impermeability the duration of elimination may reach the normal figure, but faint traces of blue may be detected in the urine for several days after the main wave of elimination has passed. The total quantity eliminated may not, however, differ greatly from the normal. Most frequently prolonged elimination coexists with a diminution in the quantity eliminated.

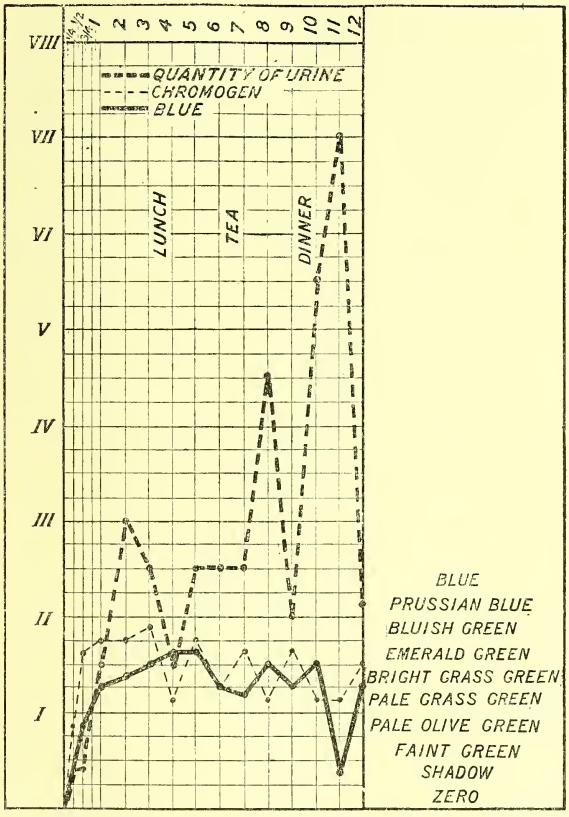
3. *The quantity of blue eliminated.*—For the purpose of quantitative estimation the chromogen must be transformed into blue in each specimen examined. The most accurate method is the comparison of the blue urine with a solution of blue of known strength, more blue being added until the depth of colouring is the same in both fluids. The yellow colour of the urine introduces a fallacy that is corrected by using the urine of the patient before the blue appeared and adding to this the standard solution of methylene blue.[17] For purposes of comparison charts may be constructed which show the varying depth of colouring of the urine and the course of the elimination. The quantity of blue eliminated is diminished in diseases of the kidney. In advanced disease no blue may appear in the urine and under these conditions chromogen may appear for a short time or may be entirely absent. In one patient under my care no blue appeared in the urine although no appreciable renal lesion was present. The patient suffered from bilharzia cystitis and took the methylene blue by mouth for its therapeutic effect. He took half a grain of methylene blue daily for a month and two grains daily for two months, but no trace of blue or chromogen appeared in the urine. In four other cases no blue was passed and each of these patients suffered from advanced renal disease. In two of these chromogen was passed and in two it was absent.

4. *Course of elimination.*—The elimination of blue rapidly rises and reaches its maximum about three or four hours after injection and remains at its highest level for four or five hours. It then falls gradually and after 30 or 40 hours has usually been reduced to a pale green tint. After this traces may be passed for some hours or even for several days. During the excretion a draught of water will cause a rapid diminution in the colour, but after an hour or so the urine resumes its previous hue. In Fig. 6 the relation of the quantity of urine and blue is shown and the cause of elimination by hourly observations during the first 12 hours in a healthy individual.

[17] Achard et Clerc: Bulletin et Mémoires de la Société Médicale des Hôpitaux, 1900.

The elimination may be intermittent. It may fall almost to vanishing point and rise again or it may disappear entirely and reappear later. Disturbances in the rhythm of

FIG. 6.



Normal elimination of methylene blue and chromogen compared with quantity of urine during first 12 hours after injection.

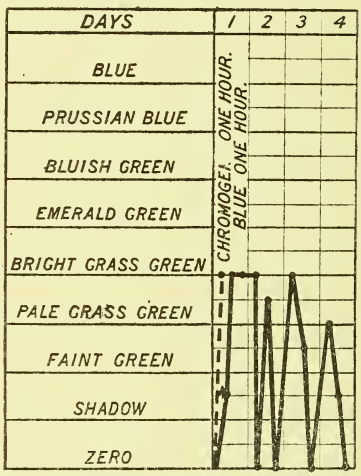
elimination occur in functional disorders of the liver. They are also said to occur in compensatory hypertrophy of the kidney. In 46 cases of different diseases Asfalg [18]

[18] Zeitschrift für Innere Medecin, 1902, p. 226.

observed intermittent excretion in 60 per cent., and in half of these it was diurnal. In 61 cases under my observation intermittent elimination was present in 14 (23·3 per cent.). In six healthy individuals the elimination was intermittent in all. (Figs. 7 and 8.)

The value of the methylene blue test in surgical diseases.— I used the test on six healthy adult men who volunteered themselves for this service. In 55 cases injections of methylene blue were made for purposes of diagnosis. The

FIG. 7.



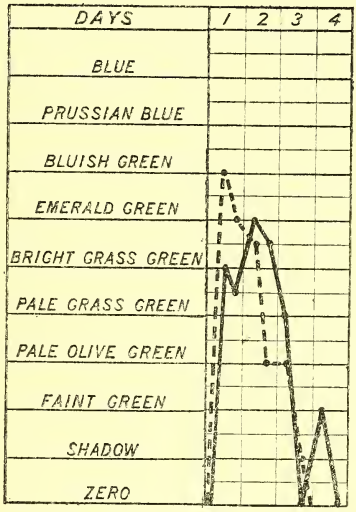
Intermittent elimination in a case of syphilis. No signs of disease of kidney. Blue shown by continuous line, chromogen by dotted line.

dose in all these cases was the same—namely, 15 minims of a 5 per cent. solution of pure methylene blue.

These cases may be briefly summarised as follows. In some conditions which were unconnected with the urinary tract an unexplained delay in the commencement of elimination was observed. In inflammatory diseases of the bladder, where there was no reason to suspect renal changes, there was also a slight delay in the appearance of the blue. Cases of obstruction in the lower urinary tract invariably showed a delayed elimination. The average time of appearance of blue in 18 cases of obstruction was 3 hours 27 minutes. The delay was more marked where the obstruction was due to enlarged prostate than where it resulted

from stricture. Thus, in eight cases of long-standing stricture the average time of commencement was two hours and 16 minutes, while in ten cases of prostatic obstruction the average delay was four hours and 25 minutes, and this did not include one case where no blue appeared. The duration of the obstruction did not sufficiently explain this difference, for the length of time during which symptoms of obstruction had been present was much greater in the strictures than in the prostatic cases. Nor was the degree of obstruction greater in the cases of prostatic disease. A similar difference was observed in the duration of the elimination of blue in

FIG. 8.



Intermittent elimination in healthy individual. Blue shown by continuous line, chromogen by dotted line.

cases of stricture and of enlarged prostate. The average duration in the former was 82 hours, not a very great increase over the normal figure, while in the cases of prostatic obstruction the average elimination continued for 118½ hours without taking the case of complete suppression of blue into consideration. In slightly damaged kidneys there was but little delay or prolongation, but where advanced renal disease was present there was delay, diminished and prolonged elimination. In severe bilateral renal disease the blue did not appear in the urine at all. There were altogether five cases in 61 where blue did not appear in the urine. One of these was

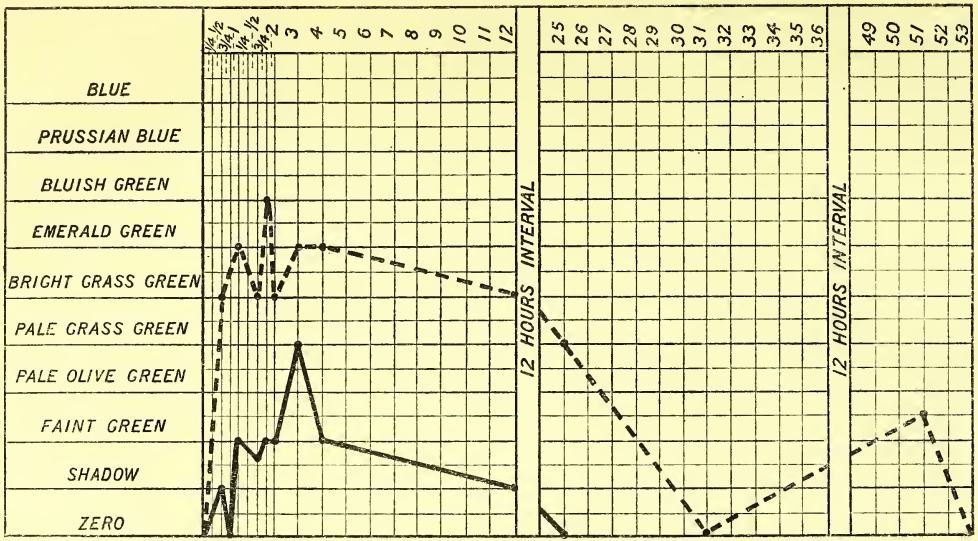
the case of bilharzia cystitis in which the kidneys were probably healthy and which I am inclined to look upon as a very unusual observation. The remaining four cases were—one case of urinary obstruction from enlarged prostate, one case of bilateral renal calculus, one case of pyonephrosis with stricture of the urethra, and one case of pyelonephritis with abscess of the prostate and foul cystitis.

I operated upon three of these cases and refused operation in one. The patient with bilateral renal calculus who was refused operation died 18 months later from suppression of urine. Of the three cases that were submitted to operation two died. On one of these the operation was done to relieve a large collection of pus in the prostate when the patient was beyond hope of recovery. The other two cases were operated with the hope of cure. The patient with enlarged prostate showed no symptoms of renal inefficiency before operation. He was a spare, muddy-complexioned man who had suffered from complete retention of urine for some months. The urine had a specific gravity of 1010. There was an increased quantity of urine and the urea varied from 0·6 to 1·1 per cent. The temperature occasionally rose to 100° F. The operation presented no difficulty and the enucleation lasted three and a half minutes. After operation the urine gradually failed and the patient died on the fifth day. The patient with pyonephrosis did not show any signs of failing renal function, but he was a heavy lymphatic man and a poor subject for operation. After nephrotomy he showed signs of commencing renal failure, but these passed off and similarly, after nephrectomy a fortnight later, there were vomiting, restlessness, distension, and diminished urine, but he recovered. The methylene blue test was again used after the nephrectomy. Blue appeared in the urine after one and a half hours and chromogen after one hour. The blue disappeared in 25 hours; the chromogen, which was present in greater quantity, pursued an intermittent course and disappeared in 53 hours (Fig. 9).

The value of methylene blue as an indication of the state of the renal function must be judged by a comparison with the information obtained from the symptoms and the examination of the urine. Three out of eight cases of stricture showed insignificant symptoms of renal inadequacy; in all the excretion of urea was large. In all of the cases there was delay and, in several, prolongation of blue elimination. The cases were selected as having suffered from intractable stricture for long periods and belonged to the class of case in which renal changes are common. In these cases the methylene blue appeared to be a more accurate test than the symptoms or the quantitative estimation of urea. In 11 cases of prostatic obstruction there were insignificant symptoms of renal inadequacy in three and fairly marked symptoms in one case. There were invariable delay and prolonged elimination of blue

The cases already quoted of complete suppression of blue

FIG. 9.



Pyonephrosis. Chart of elimination of blue (continuous line) and chromogen (dotted line) after nephrectomy. Neither blue nor chromogen appeared in the urine in a previous test before nephrectomy.

when no symptoms of renal inadequacy were present may be taken as a type of the more accurate indication of the renal function by methylene blue. Further, the comparison of the result of the blue test in these prostatic cases with that of the stricture showing a less efficient renal function in cases of enlarged prostate than in stricture which was not shown by the symptoms is borne out by clinical experience of such cases. In two of the cases of kidney disease there were general symptoms of renal inadequacy; in one this was only continuous thirst, in the other the symptoms were well marked. In these cases no blue was passed. In the other two cases where no symptoms of renal failure were present and no blue was passed one died after the operation and had advanced interstitial changes in the kidneys and the other developed grave symptoms of renal failure after the operation, but these passed off. In one case there was a very marked improvement in the elimination of blue after the removal of a large pyonephrosis and this was attributed to the removal of a reno-renal reflex inhibition. The test is, I believe, one which is more trustworthy than the quantitative examination of the urea or the general symptoms of renal inadequacy. And this is especially the case in the more severe grades of kidney disease. In the slighter grades of renal disease the blue test appears to give results that are somewhat variable.

It has been urged in criticism of this method that the formation of chromogen introduces an element of uncertainty into the test. The chromogen should be converted into blue when the quantity of the dye is estimated. The elimination of the blue by the liver appears to me to be a more serious disadvantage and one which cannot be overcome. Lépine[19] has drawn attention to a fallacy which underlies observations on this and similar methods. The kidney does not eliminate all bodies without distinction in the same manner, and data obtained from the elimination of one body may not be reliable when applied to another. It is undoubted, however, that there is a certain parallelism in the elimination of different bodies and that the general permeability of the kidney for most bodies which it excretes is approximately similar to that of methylene blue.

(*b*) *The Toxicity of the Urine.*

Professor Bouchard introduced the method of estimation of the toxicity of the urine as a means of determining the efficiency of the kidney to eliminate the poisons produced by metabolism. This method attributes to the kidney as its most important function the removal from the blood of certain substances which, if retained, would cause uræmia.[20]

[19] Lyon Médicale, 20 Février, 1898.
[20] Hallion et Carrion: Presse médicale, 30 Juin, 1900, p. 321.

The normal urine is highly poisonous but the exact nature of the poison is unknown. The injection of a certain quantity of urine into a rabbit causes symptoms of poisoning and death after a varying interval. The lethal dose of normal urine for rabbits is stated at from 40 to 50 grammes per kilogramme of body-weight. Retention in the body, or increased excretion in the urine, of poisonous substances will cause variation in this dose. Most observers who have used the method agree that it is likely to afford useful information if the toxicity of both the urine and blood be examined, but that it is open to many fallacies and cannot be judged with mathematical exactness.

3. *The Glandular Function of the Kidney.*

Phloridzin test.

Mering [21] discovered in 1885 that the injection of phloridzin caused a temporary glycosuria of a few hours' duration. The amount of sugar excreted does not depend upon the dose of phloridzin, provided sufficient of the drug be given to produce the maximal effect. The source of the sugar is apparently the tissue protcid. The phloridzin glycosuria is renal in origin as the experiments of Zunz,[22] Biedl, and Kolisch [23] have shown. Klemperer [24] was the first to apply this method to clinical medicine. He showed that phloridzin glycosuria did not appear in cases of chronic nephritis. Achard and Delamere [25] introduced the drug as a test of the renal function and brought its use within the range of practical medicine. These observers showed that the sugar production was dependent upon the functional activity of the kidneys, and any variation must indicate a departure from the normal functions of the kidneys.

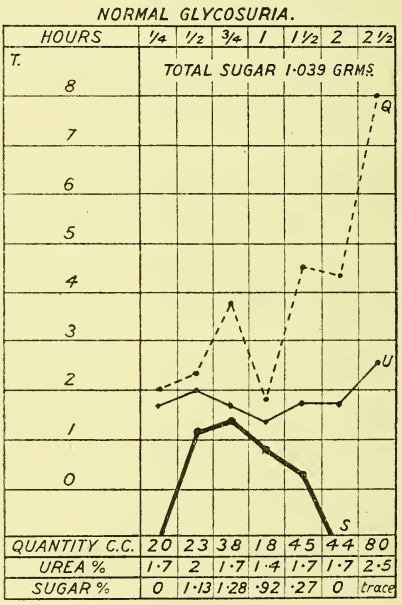
Technique of the phloridzin test.—A subcutaneous injection of 15 minims of phloridzin solution (1 in 200) is made. This corresponds to five milligrammes of phloridzin. In a healthy individual sugar appears in the urine in from 15 to 30 minutes and the glycosuria continues for from two to four hours. The most important factor in the test is the total quantity of sugar eliminated. This varies from one to two grammes. The lowest limit of normal glycosuria lies between 50 centigrammes and one gramme and the highest from 2 grammes to 2·50 grammes. In the accompanying chart

[21] Centralblatt für die Medicinischen Wissenschaften, 1885, S. 531.
[22] Verhandlungen der Physiol. Gesellsch. zu Berlin, 1894, S. 51.
[23] Quoted, Pavy, Brodie, and Siau: Journal of Physiology, 1903, p. 467.
[24] Verhandlungen der Verein für Innere Medicin, Mai, 1896.
[25] Bulletin et Mémoires de la Société Médicale des Hôpitaux, p. 381, 1899.

(Fig. 10) the normal course of the elimination of sugar after an injection of five milligrammes of phloridzin is shown. The curves of quantity of urine and urea also appear on the chart. Delay in the appearance of the sugar or prolongation of the elimination to five or six hours as slight traces are not signs of abnormal function.

Variation in the phloridzin diabetes of normal kidneys.— Achard and Delamere have shown that a diminution of the

FIG. 10.

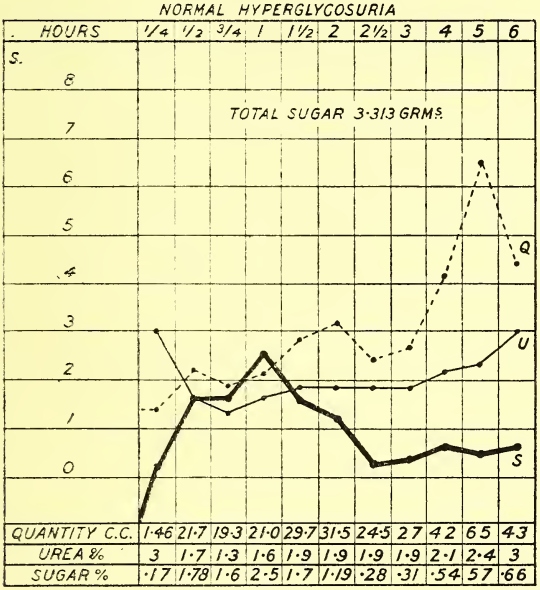


Sugar shown as dark continuous line (S), urea as faint continuous line (U), and quantity as dotted line (Q). Observations made every quarter of an hour for one hour and every half hour after that.

quantity of sugar eliminated (hypoglycosuria) or an excessive diabetes (hyperglycosuria) may take place without anatomical changes being present in the kidneys. Normal hyperglycosuria is more frequently observed in healthy individuals than a diminished secretion of sugar. It has been met with under the most varying conditions, such as typhoid fever, acute articular rheumatism, and bronchitis. In two healthy adults, under exactly similar conditions, the

hypodermic injection of five milligrammes of phloridzin produced a glycosuria in the first which commenced in 15 minutes and lasted six hours, with a total elimination of 3·313 grammes of sugar (Fig. 11), and in the second a glycosuria which commenced in 30 minutes and lasted two and a half hours, and 1·039 grammes were eliminated (Fig. 10). The first was a hyperglycosuria, while the second was a normal glycosuria.

FIG. 11



HOURS	1/4	1/2	3/4	1	1½	2	2½	3	4	5	6
QUANTITY C.C.	1·46	21·7	19·3	21·0	29·7	31·5	24·5	27	42	65	43
UREA %	3	1·7	1·3	1·6	1·9	1·9	1·9	1·9	2·1	2·4	3
SUGAR %	·17	1·78	1·6	2·5	1·7	1·19	·28	·31	·54	57	·66

Excessive quantity of sugar after injection of five milligrammes of phloridzin. Healthy subject. Sugar indicated by thick continuous line, urea by thin continuous line, and quantity of urine by dotted line.

Phloridzin test in renal disease.—The important variations found in renal disease are either a diminution of the quantity of sugar below one gramme or a complete absence of the sugar ; a normal glycosuria has rarely been observed. Two examples occur amongst Delamere's cases,[28] and three cases are described by Jouffray.[27] Albarran has met with

[26] Thèse de Paris, 1899. [27] Thèse de Lyon, 1903.

several instances of marked hypoglycosuria with insignificant lesions of the kidney. This observer has also recorded instances of hypoglycosuria in unilateral renal lesions where the second kidney was functionally perfect by other tests.

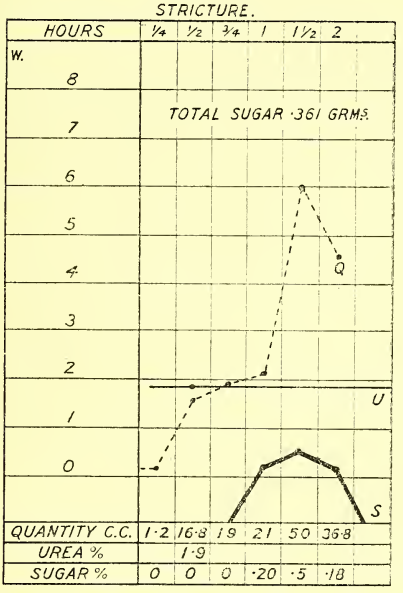
Among my cases was one of renal colic in which the total glycosuria amounted only to 0·53 gramme, and another of moveable kidney in which the glycosuria was 0·61 gramme. In two cases there was hyperglycosuria. In one I had recently removed a tuberculous kidney and there still remained severe tuberculous cystitis, but the solitary kidney was healthy. In this patient 5·21 grammes of sugar were rapidly eliminated, commencing half an hour after the injection. In the second there was chronic pyelonephritis more marked on one side. There were periodical exacerbations and the general symptoms pointed to a failing renal function. The patient passed 3·40 grammes of sugar in two hours. The quantity of sugar was diminished in cases of moveable kidney, renal colic, vesical calculus with slight pyelitis, enlarged prostate with interstitial changes in the kidneys, tuberculous kidney, and intermittent pyuria of obscure origin.

The value of the phloridzin test.—A diminished phloridzin glycosuria indicates in most cases disease of the kidney, and a complete absence of sugar should be regarded as a sign of advanced renal disease. The cases to which I have referred point in this direction and the conclusions were supported by other evidence. Sugar was entirely absent in four cases: a patient with a damaged solitary kidney after nephrectomy for pyonephrosis, another with obstructive oliguria which became anuria, and two cases of enlarged prostate with urostasis. In these there were no symptoms pointing to renal inadequacy in the solitary kidney case and in one case of enlarged prostate. In the case of oliguria there was the diminished urine but no general signs at the time of the test, and in the enlarged prostate the signs of renal inadequacy were well marked—there were dry glazed tongue, thirst, headache, marked loss of flesh, loss of appetite, and nausea at times. The former case was under my colleague, Mr. J. G. Pardoe, and he kindly permitted me to examine the patient and to watch his progress. In the case of solitary kidney the patient had shown signs of renal inefficiency immediately following the operation of nephrectomy but these had subsided. The urea amounted to 1 per cent. and 1·2 per cent. on two separate examinations of 24 hours' specimens.

I have already referred to the case of enlarged prostate in considering the methylene blue test. The patient showed no symptoms of renal inefficiency with the exception of a moderate polyuria. The total urea excretion was well up to normal. No phloridzin glycosuria was observed. The patient died from suppression of urine after prostatectomy and his kidneys showed advanced interstitial changes and

were hollowed from pressure. In the second case of enlarged prostate there were symptoms of renal inadequacy. After a period of bladder drainage the symptoms were less marked and the injection was repeated. On this occasion a reduced quantity (0·303 gramme) of sugar was eliminated. After prostatectomy the patient was drowsy for three days but his urine was plentiful and he made an excellent recovery. There was diminished glycosuria without symptoms of renal disease in several cases where it seemed improbable that the

FIG. 12.



Diminished and delayed elimination of sugar in case of stricture.

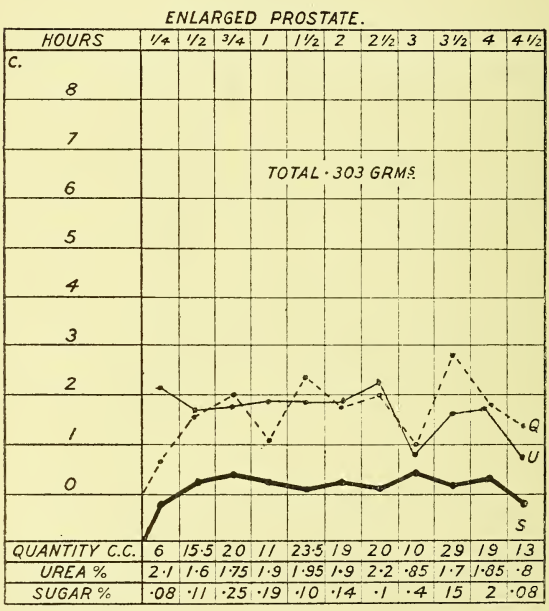
renal function could be impaired. Thus in a case of moveable kidney the excretion was 0·614 gramme. In obstruction from stricture (Fig. 12) or enlarged prostate (Fig. 13) there was diminution of the glycosuria.

Compared with the urea output and the general symptoms of renal inadequacy the phloridzin test was more delicate in these cases. The fallacy to which it is specially open is the pronounced effect which minor renal changes may produce upon the glycosuria. It is possible that this fallacy may be

overcome by the use of larger doses of phloridzin, as Albarran has suggested.

I have indicated the fallacies and difficulties connected with each of these methods. As a measure of the tota renal function the phloridzin and methylene-blue tests are most trustworthy. The phloridzin method is open to the

FIG. 13.



Diminished and prolonged elimination of sugar in case of enlarged prostate.

objection that it is too easily influenced by slight variations in the renal function. At the present time the methylene-blue test is the method by which most trustworthy information can be obtained and appears to me to form a valuable addition to the clinical methods of estimation of the renal function.

LECTURE II.

Delivered on March 4th, 1907.

The Estimation of the Function of One Kidney

Mr. President and Gentlemen,—In my first lecture I endeavoured to show what means had been adopted to ascertain the value of the combined function of the kidneys. I shall now pass to the consideration of the methods at the disposal of the surgeon in estimating the function of one kidney. When one kidney is diseased and it is accepted that its function is seriously impaired or totally destroyed the question of prognosis and the decision in regard to surgical interference and its extent will in a considerable majority of cases depend upon the view which the surgeon takes in regard to the functional activity of the second kidney. I shall briefly review the methods upon which until a recent date the surgeon relied for the data on which to base his judgment in this matter.

Where one kidney is obviously diseased the patient may show symptoms of failure of the renal function and thus betray the reduced activity of the second kidney. With these symptoms before him the surgeon will be able to decide whether he will take the risk of advising surgical interference and how far this may be carried. But it is in the case where general symptoms of renal failure are absent that more information is desired in regard to the functional power of the second kidney. The surgeon has hitherto had to depend upon the presence of local signs of disease of the second kidney, upon his experience of the pathology of such diseases, and lastly upon statistics. There may be enlargement, pain, and tenderness of the organ, but these do not give unquestionable proof that the kidney is seriously diseased. The x rays may give valuable aid in some cases of calculous disease. Extensive shadows in the second kidney may indicate that the margin of renal tissue is too small to maintain the function, or, on the other hand, the absence of shadows will show that calculi are not present in the second kidney.

But these form only a small number of the cases that are presented for consideration. The real difficulty arises when there are no general symptoms of renal failure and there are no local signs of disease of the second kidney. It cannot be said in such a case that the absence of signs of disease are a

proof of the health of the second kidney, for experience has abundantly shown this to be erroneous.

The statistics which have been compiled with regard to the bilateral incidence of various renal disorders may be used in this service. Some of these are seen in the following list :—

Statistics of Solitary Kidneys and Bilateral Renal Disease.

Solitary kidneys (one kidney atrophied)	6 in 15,904, 1 in 2650 (Morris).
Small, shrunken, or wasted ...	59 in 8178, 1 in 138 (Morris).
Malignant growths, bilateral ...	12 in 118, 1 in 10 (Kelynack).
Polycystic kidney, bilateral ...	150 in 191 (Küster, collected). 25 in 26 (Dickinson, collected). 65 in 66 (Lejars, collected). 4 in 4 (Israel). 3 in 7 (Morris).
Calculus, bilateral	38 in 76, 50 per cent. (Legueu). 90 in 764, 11·78 per cent. (Küster). 21 in 83, 25·3 per cent. (Torrés).
Pyelonephritis, bilateral	59 in 71, 83 per cent. (Weir).
Tuberculous disease, bilateral ...	43 in 81, 53 per cent. (Heilberg and Oppenheim). 106 in 205, 51 per cent. (Pulet).

Statistics have, however, only a limited value. It will be seen by referring to the figures quoted above that renal growths are unilateral in over 89 per cent. of published cases. This percentage is therefore accepted as a guarantee that in removing a kidney containing a renal growth little or no risk is run of the patient having submitted to a useless operation from the presence of a second tumour in the remaining kidney. Again, it is known that the ratio of solitary kidneys is 1 in 2650 cases and that a kidney may be removed with but small chance of the patient being dead from uræmia in a few days from the removal of his entire urine secreting apparatus. Apart from such unusual cases, however, there is a large number of patients who suffer from some renal disease which is notoriously bilateral in its later stages. These cases include certain forms of renal calculus, tuberculous disease, and suppurative diseases of the kidney. In operating upon the obviously diseased kidney in such conditions and especially in proposing removal of the organ a certain risk is undertaken.

I have collected from the literature 75 cases of operation upon one kidney where uræmia or anuria commenced within the first few days after operation. Of these 26 (34·6 per cent.) were calculous, 17 (22·6 per cent.) tuberculous, and other suppurative conditions were present in 13 (17·3 per cent.). Nephrotomy was performed in 27 cases and nephrectomy in 48. There was no second kidney in five. The second

kidney was atrophied in seven, the seat of nephritis or degeneration in 18, calculus in 12, pyo- and hydronephrosis in nine, tuberculosis in six, and new growth in two. It is certain that in some of these cases operation would not have been performed had the state of the second kidney been known.

Cystoscopic Examination of the Ureteral Openings.

The discharge of urine or other material from the ureteric orifice might be expected to give valuable assistance in the investigation of renal disease, and this is the case where the localisation or diagnosis of an obscure disease is the subject of inquiry. But when the diagnosis is already made and the sole object of investigation is to measure the functional activity of the kidney the information gained by the examination is frequently disappointing.

The absence of a periodic discharge of urine does not signify that no kidney is present or that the functional power of the kidney is destroyed. It not infrequently happens that no discharge of urine is observed for a considerable time when there is every reason to believe that the kidney is healthy. Such periods of functional inactivity are the result of nervous influences. Where one kidney is absent it does not of necessity follow that the ureteral opening is also absent. In a case recorded by Jolly [1] the right kidney was absent. On the right side of the trigone there was a ureteral opening into which a probe could be passed for 1 centimetre and beyond that there was a fibrous band 13 centimetres long. Usually, however, when one kidney is congenitally absent there is no ureteral opening on that side. The remaining ureter may be normal in position or it may be displaced. In 18 cases where one kidney was absent the corresponding ureter was also absent in 12, and it was specifically stated that the ureteral orifice was absent in four of these.[2] It will sometimes happen from various causes that there is a difficulty in finding one ureteric orifice in cases where both kidneys are present.

A copious efflux is not a guarantee that the function of the kidney is healthy. The polyuria of advanced interstitial nephritis and of waxy disease may be observed on the side of the second kidney in renal surgery. A purulent or bloody urine is no measure of the renal function, however important it may be in diagnosis. I have never seen a "solid efflux" of blood and débris such as Mr. E. Hurry Fenwick describes,[3]

[1] Soc. Anat. de Paris, Jan. 9th, 1896.

[2] In these cases the genital system was either normal or no abnormality was mentioned in 15. There was general malformation of the external genital organs in one case and abnormality on the same side as the absent kidney in two.

[3] Ureteric Meatoscopy in Obscure Diseases of the Kidneys, 1903.

but I have met with a case of hæmaturia in which an irregular greyish spongy-looking clot projected from the left ureter (Fig. 14). The renal function was not seriously mpaired. It is a different matter when a worm of semi-solid waxy pus is slowly expressed at intervals from a reddened ureter (Fig. 15). I have notes of two such cases. There had been symptoms of renal trouble for eight and 11 years respectively and in each case the kidney was a large thick-walled pyonephrosis containing much semi-solid pus, débris, and calculi. This form of ureteric discharge is significant of a functionless kidney.

I have met with four examples of a condition which Mr. Fenwick has described as the "dragged out" ureteric orifice.

Fig. 14.

Ragged greyish blood clot projecting from left ureter after severe renal hæmaturia.

Of the condition this observer says: "It affords the most conclusive *cystoscopic* evidence that we possess of the partial destruction of a small, often unfeelable, kidney by tuberculosis." The orifice is displaced upwards and outwards and lies in the depth of a tunnel-like depression. In the four cases that came under my observation there was advanced tuberculous disease of the kidney in all. In one case the hypertrophied inter-ureteric bar which formed a ridge running along the floor of the tunnel was dragged in and out at each respiratory movement almost like a piston; in another no respiratory movement took place but pressure on the kidney caused a violent tug at this ridge of muscle.

Chromocystoscopy.

A method of cystoscopic estimation of the renal function has been suggested by Vallicher and Joseph.[4] An intramuscular injection of four cubic centimetres of a 4 per cent. solution of indigo-carmine is made. Elimination commences in 20 minutes, reaches its height 30 minutes later, and has ceased in two hours. The authors claim that the examination of the ureteral openings and the observation of variations in the depth of staining of the urines during the elimination will afford an approximate idea of the functional value of the two kidneys (Fig. 17). Similar observations had previously been made with methylene blue. This method is preferred by some (Hartmann, Legueu) to the results of ureteral catheterisation. The two methods do not, however, lend themselves to comparison. Differences in the depth of staining of the urine of each kidney can be observed by either method, but much more accurately in collected separate urines than by watching the momentary jet from the ureteral orifice. But in addition to this the chemical and microscopical analysis of the separated urines gives invaluable information that cannot be obtained by chromocystoscopy. At the best it is a ready clinical test of the presence or absence of a ureteral efflux and from the opacity of the jet

Fig. 15.

Mass of semi-solid pus expressed at intervals from left ureter. Case of left pyonephrosis.

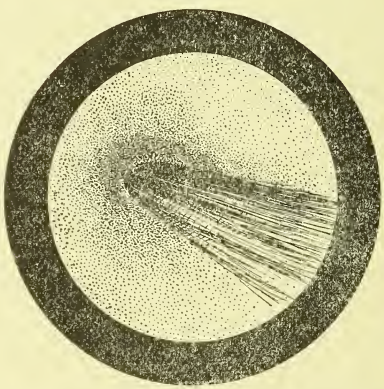
[4] Münchener Medicinische Wochenschrift, 1903, p. 2028, and Deutsche Medicinische Wochenschrift, 1904, p. 536.

some idea may be gained of the function of the kidney. As a means of localising the position of the ureters in difficult cases and of making observations on the renal secretion where catheterisation of the ureters or separation of the urines is impossible it may play a minor rôle.

Methods of Obtaining the Urine of Each Kidney Separately.

It has been the ambition of surgeons almost since the date of the first nephrectomy to obtain the urine of each kidney separately for examination. Dr. Tuchmann [5] perfected his

Fig. 16.



"Dragged out" ureter in case of renal tuberculosis.

apparatus five years after Simon's nephrectomy and other methods were published in rapid succession. So far as the earlier attempts were concerned the chief source of interest was the localisation of disease to one or other kidney. Other means have been introduced and perfected which have to some extent, although not entirely, replaced this use of the separation of urines, and its chief sphere of usefulness at the present time is the examination of the urines in order to estimate the function of these organs.

It is beyond the scope of these lectures to trace the evolution of the methods of separation of the urine from each kidney, nor shall I discuss the technique or dwell upon

[5] Wiener Medicinische Wochenschrift, 1874, pp. 21-22.

the arguments for or against this method of investigation. We are concerned here with the results obtained by different methods of testing the renal function.

The Examination of the Urines of the Two Kidneys.

The cumulative evidence of many series of careful examinations have provided a quantitative average for the combined output of the two kidneys. With the separation of the urine into the output of each kidney the necessity for a new standard for comparison arose. It was not sufficient to divide the total output by two in order to indicate the work of one kidney, for Landois,

Fig. 17.

Chromocystoscopy. The left ureter is shown at the moment when a jet of urine stained with indigo-carmine is being expelled.

Hermann, Ludwig, and others have shown the unequal physiological value of the kidneys at a given time in animals.

For reasons that I shall presently relate the urine of the second kidney, when one is diseased, cannot always be used as a normal standard with which to compare the work of the diseased organ. An independent normal standard must therefore be set up to show the average normal output of one kidney. This standard has been provided by the work of Albarran.[6] According to this observer no regular alternation is observed in the work of the two kidneys, but when the secretion of each kidney is collected during six or 12

[6] Exploration des Fonctions Rénales, 1905.

hours it is found that each has performed nearly the same work. One may consider as practically healthy a kidney which secretes a urine like the following in 24 hours :—

Quantity	600 to 700 cubic centimetres.
Urea	12 to 15 grammes.
Chlorides	5 to 6 „
Δ	− 1·30° to − 1·50° C.

If the time during which the urine is collected is only two or three hours the figures are less reliable. It is then necessary to study the urine at a time when digestion is not going on and when the individual has not drunk anything for several hours.

Albarran gives the following as an analysis of urine collected from one kidney during one hour under these conditions when both kidneys are healthy :—

Quantity	50 to 60 cubic centimetres.
Δ	− 1·20° to − 1·50° C.
Urea	12 to 17 grammes per litre.
NaCl	10 to 12 „ „

In comparing the function of two healthy kidneys this observer found that when the comparison was made of urine collected during so short a time as a quarter of an hour the difference amounted to as much as from 10 to 30 per cent. in the quantity of urine secreted, but when the examination was extended to one hour the difference was reduced to 10 per cent. The difference in the quantity of urea might be one gramme per litre or might amount to 6·50 grammes. The difference in the quantity of chlorides amounted to 50 centigrammes per litre and might attain five grammes. The diseased kidney usually secretes less urine than its healthy or less diseased neighbour. This will in some manner depend upon the form and extent of the disease. A hydronephrotic kidney will pass no urine through the catheter or only a very small quantity during the period of its retention. A pyonephrosis or an extensive pyelonephritis will produce a much reduced quantity. This reduced activity may be thrown into stronger relief by the secretion of an increased quantity of urine by the healthy organ and an erroneous idea of the extent of the disease may be gained by observing the inequality of secretion in such a case. The polyuria may result from passing causes or it may result from compensatory hypertrophy.

But there are frequent exceptions to this statement. The two urines may be practically equal in quantity where one kidney is diseased. Further, as Albarran has pointed out, there may be an exaggerated activity on the part of the diseased organ so that a polyuria may be observed on this side. There may be at the same time an excessive elimination of urinary salts. The urine of the diseased side is often lacking in pigment. This may be observed when the quantity of urine does not show a very great difference from that of

the healthy kidney; it is more striking where the quantity of urine is excessive on the diseased side. There is usually a diminution in the quantity of urea, chlorides, and phosphates contained in the urine of the diseased side, and this is greater when the disease is more advanced. The following analysis of the urines from a case of calculous pyonephrosis illustrates this and other points to which I shall refer later.

	Right kidney (diseased).	Left kidney.
Quantity	206·5 c.c.	107·5 c.c.
Specific gravity	1004	1011
Δ...	−0·18° C.	−0·76° C.
Colour	Pale limpid.	Fairly coloured.
Urea	0·4 per cent.	1·3 per cent.
Uric acid	0·0067 ,,	0·0150 ,,
Chlorides as chlorine ...	0·09777 ,,	0·1112 ,,
Phosphates as P_2O_5 ...	0·08 ,,	0·034 ,,
Methylene blue	No change in colour.	Appeared 1 hour 50 minutes, green colour, duration 18 hours.
Chromogen appeared ...	25 minutes, faint green.	25 minutes, deep green.
Phloridzin glycosuria ...	0·395 grammes.	1·623 grammes.

Cryoscopy of the Two Urines.

Changes in the freezing point of the two urines are dependent upon a proportional increase or decrease of the molecular composition of the urine. In order to make observations of any value upon the cryoscopy of the urines a knowledge of the comparative volumes of the urines is necessary. Just as in estimating the total function of the kidneys the volume of urine and its molecular composition change under varying conditions during the day and night, so the composition of the single kidney urine will change, and an attempt to estimate the functional value of one kidney must be subject to similar restrictions. Thus it is necessary to collect the urines by catheters during 24 hours and to examine the mixed specimen, and, further, the observations should be repeated on several successive days. It is evident that such a method of examination is impracticable, so that observations must be made, if cryoscopy is to be used, upon a urine secreted during a much shorter period of time (two or three hours). The variations in healthy individuals, even with a careful control of the solid and fluid intake, are very considerable, and it appears to me to be doubtful whether any trustworthy data in regard to the function of one kidney can be obtained by this method.

Comparative cryoscopy of the two urines will, however, give some information in regard to the difference of function between the kidneys and, if it can be ascertained that one of them is healthy, this may act as a standard for comparison for the other. It must be remembered, however, that the function of the healthy kidney is likely to be depressed from

the presence of its diseased neighbour. Usually there is a diminished quantity of urine with a reduced molecular content on the diseased side; occasionally there may be a polyuria with a proportionally greater reduction of molecules. The presence of polyuria or the reverse is not a measure of the functional activity of the kidney, and even where the quantity of urine is included in the formula the large variations are likely to prove a fallacy in the result of the calculation. It is important, also, to note that the healthy or almost healthy kidney may produce an increased quantity of urine. The result may be affected by these factors, so that even when the freezing point, corrected for volume, of the two sides is compared higher figures may be obtained on the diseased side.

When the volume of urine of one kidney is greater and the freezing point shows at the same time a greater molecular content this kidney is functionally more active than its neighbour.

In the lesser degrees of renal disease the cryoscopy figures are not usually altered, but where disease has destroyed a large part of a kidney there is usually a marked difference between the freezing points of the two urines. The variations in the point Δ of the two urines do not follow closely those of the quantity of urea, sodium chloride, and phosphates.

Methylene Blue Test for Each Kidney.

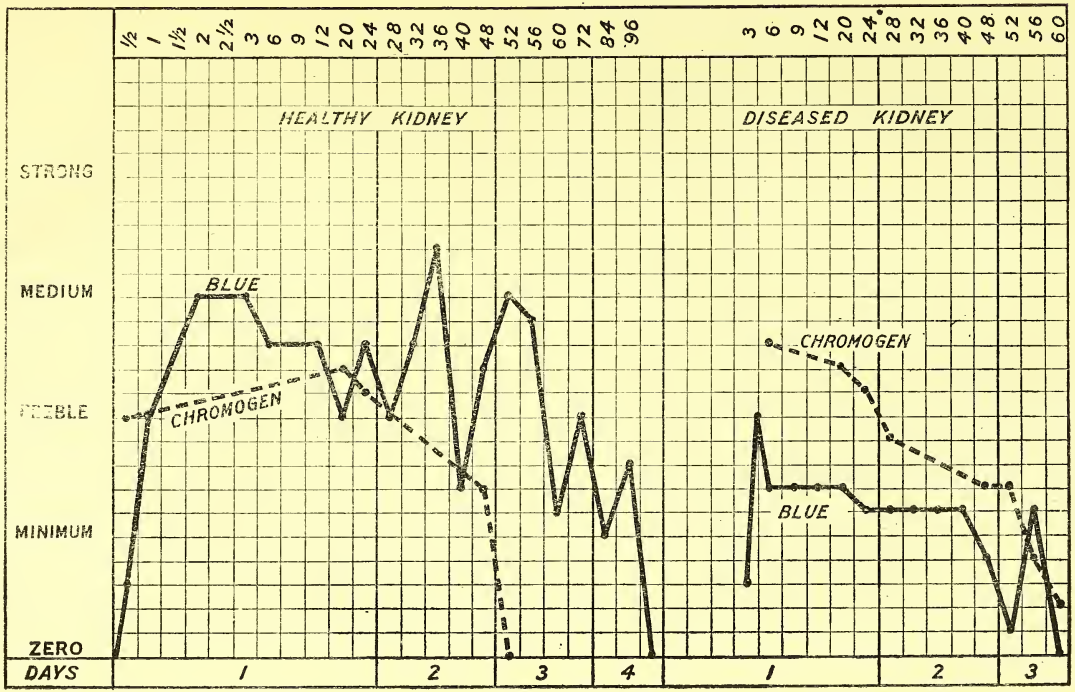
In using methylene blue for the estimation of the function of each kidney it is obviously inadvisable to make observations for the 60 or more hours during which the blue may be expected to be present in the normal state, much less is it expedient to attempt the drainage of each kidney during the protracted elimination that may occur in disease. The accompanying chart (Fig. 18) shows the elimination of blue and chromogen in a case of hydronephrosis.

Two of the important points in the elimination of methylene blue by the kidneys may, however, be investigated with a comparatively short ureteral drainage. Observations may be made on the time of appearance of the blue and chromogen and the depth of staining of the secretion as a measure of the quantity of blue eliminated. For this purpose a catheterisation of an hour, or at most two hours, will suffice.

I have selected the following cases in illustration as they indicate the extent of the information that may be gained by this method and show how far the conclusions based upon it were justified.

Case 1.—The patient was a man suffering from right-sided pyelitis of ten months' duration with an enlarged tender kidney. On the right (diseased) side methylene blue

FIG. 18.



Elimination of methylene blue and chromogen in a case of hydronephrosis. Delay and diminished quantity of blue and delay of chromogen on diseased side (Albarran).

appeared in 60 minutes as a dirty green colouration and the microscope showed pus and renal cells and bacilli. The left ureter gave clear blue urine in 30 minutes which showed no deposit. After nephrotomy the symptoms subsided.

CASE 2.—The patient, aged 48 years, came under my observation at the North-West London Hospital. There was a large, hard left kidney and the right kidney was not palpable or tender. The left (diseased) kidney excreted no methylene blue and no chromogen and the right urine was deeply stained with methylene blue and chromogen in 27 minutes. A large thin-walled pyonephrotic cyst containing masses of calculi was removed. The patient died with symptoms of septic absorption. The remaining kidney (right) was found to be healthy.

CASE 3.—In this case there was a large, hard, irregular calculous mass in the right kidney and the left kidney was not palpable or tender. There were no symptoms of renal failure except constant thirst. No blue or chromogens appeared in the urine from either kidney. Operation was refused and the patient died from suppression of urine 18 months later. The left kidney was also destroyed by calculi.

CASE 4.—This was another case of calculous pyonephrosis. The right (diseased) kidney passed no blue but a small amount of chromogen appeared. The left kidney passed chromogen in quantity in 25 minutes and blue in 1 hour 50 minutes. The right kidney was found on operation to contain large calculous masses with a thin covering of fibrous renal tissue. The patient made a good recovery.

An early onset of elimination and a good quantity of blue in the urine were accepted in my cases as a guarantee of the functional activity of the second kidney, whereas the absence of blue and chromogen in the urine of the second kidney was taken as an indication of an inefficient or destroyed kidney. Between the extremes of a well-marked blue elimination and its complete absence from the urine of the second kidney there are varying degrees of elimination. In making observations upon such cases the methylene blue method suffers from the disadvantage of a long duration. The drainage of each ureter by catheter during a period of two or three days is impracticable as a routine measure.

Except in such pronounced results as those which I have related the method does not provide sufficiently definite information on which to base conclusions as to the total function of one kidney. But as a means of comparing the work of the two kidneys in a given time it has an undoubted value. If the function of the combined kidneys is estimated at a high value and the separation of the urines shows that the blue is secreted with little delay on either side and in about equal

quantity the active renal tissue is probably distributed pretty evenly between the two organs and is present in good quantity. If, on the other hand, the commencement of elimination is delayed and the total blue excreted is small in amount and by draining each kidney the proportion is found evenly distributed between the two, it would be inferred that a diminished amount of renal tissue was distributed equally between the two organs and for this reason nephrectomy might be contra indicated. When the difference between the two secretions is marked so that the supposed healthy kidney secretes much the greater quantity of methylene blue it will appear probable that the second kidney has already assumed a large part of the renal function and may be trusted to carry it on if the diseased organ is removed. This demonstration of the renal function will be the more striking if the diseased kidney eliminates no trace of blue or chromogen. On the other hand, it is certain that if the second kidney is the seat of latent disease which has hitherto passed unnoticed examination of the urine drawn by catheter from that ureter will give a clue to the presence of the disease which will be strengthened by the use of the methylene blue test. I have not observed as a frequent occurrence the intermittent elimination of methylene blue by the healthy second kidney which Albarran attributes to compensatory hypertrophy.

Before leaving this test an observation may be made in regard to the demonstration of the relief from the reno-renal reflex. In a case of pyonephrosis nephrotomy was performed on August 16th, 1906, and the injection of methylene blue failed to colour the urine or to appear in the discharge from the wound. Chromogen appeared in the urine in one and a quarter hours. Nephrectomy was performed on August 29th and the methylene blue test was again carried out. The dye now appeared as a deep green and the chromogen as a blue-green in the urine in one and a half hours and one hour respectively. The patient made a good recovery. (Fig. 9, Lecture I.)

Phloridzin Glycosuria Test for each Kidney.

In healthy individuals the elimination of glucose by the two kidneys is equal and parallel. Variations in the work of the two organs occur, however, which may amount to from 10 to 20 per cent. I have observed a difference of 0·45 gramme between the amount eliminated by each kidney (1·20 right and 1 65 left) in a healthy individual. Albarran gives the following results in four healthy individuals:—

	Right kidney.	Left kidney.
1.	0·86 gramme.	0·68 gramme.
2.	1·20 ,, ...	1·14 ,,
3.	1·66 ,, ...	1·21 ,,
4.	1·80 ,, ...	1·62 ,,

The elimination of sugar commences in a healthy kidney in the first half hour and most frequently the first appearance of it is observed in from 15 to 20 minutes after the injection. The kidneys commence simultaneously to eliminate the sugar and cease almost at the same time. Elimination continues about one and a half to two hours, but may be more prolonged.

FIG. 19.

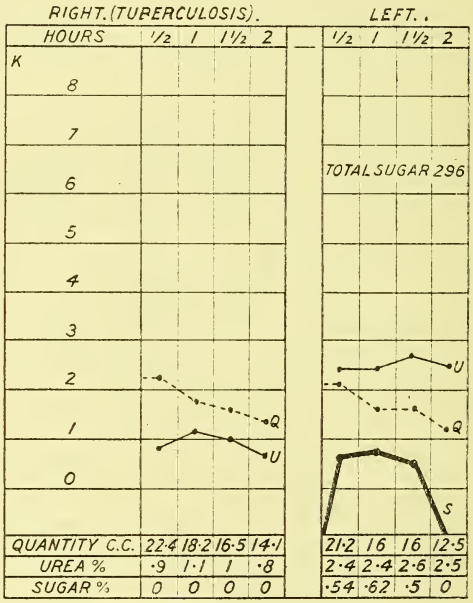


Chart of work of each kidney in case of advanced tuberculosis of right kidney. Absence of sugar on diseased side. Sugar indicated by thick continuous line, urea by thin continuous line, and quantity of urine by dotted line.

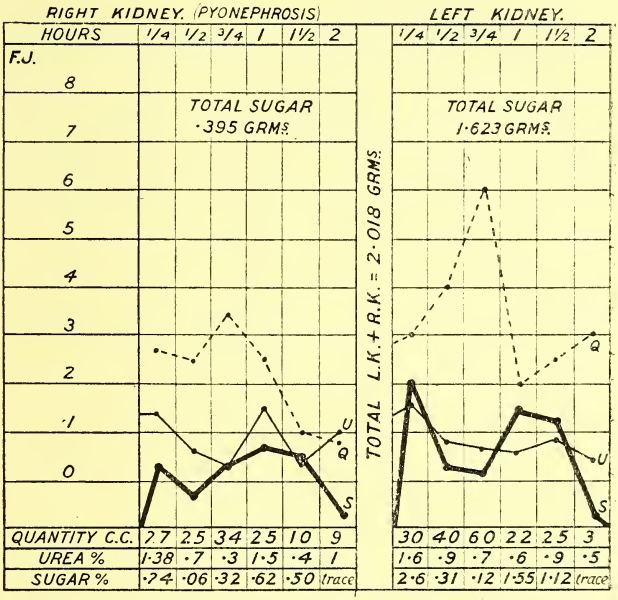
When one kidney is diseased there may be complete absence of sugar on that side, while the sugar eliminated by its healthy neighbour may represent the share normally taken by one kidney, leaving a reduction of the total sugar in the mixed urines; the total amount may not be reduced, since the healthy kidney may eliminate a quantity equal to two kidneys, or the second kidney may eliminate a diminished quantity of sugar, so that the total sugar is much reduced. Usually the quantity of

sugar is diminished on the diseased side and normal on the healthy side. Rarely a hyperglycosuria may be observed on the diseased side.

The following case may be referred to fully, for it has points of interest in diagnosis as well as in the estimation of the renal function.

The patient, aged 54 years, was admitted to St. Peter's

FIG. 20.

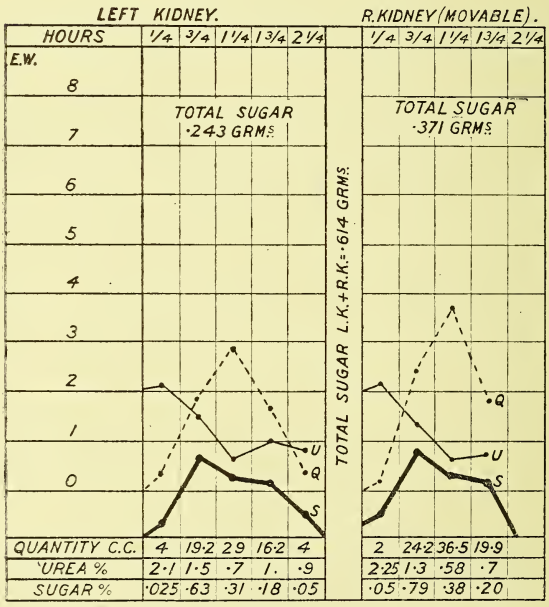


Large calculous pyonephrosis. Diminished elimination of sugar on diseased side.

Hospital under my senior colleague, Mr. P. J. Freyer. In his absence it fell to me to examine the bladder with the cystoscope and he kindly permitted me to make further observations upon the patient in regard to his renal function. There was a history of frequent micturition during the day and night for months and scalding during the act. There had been difficult micturition and a poor stream for six weeks but never hæmaturia. The kidneys were not tender or painful and neither

kidney could be felt under deep anæsthesia. Tubercle bacilli were detected in the urine. Vesical spasm rendered cystoscopy difficult. The bladder showed general subacute cystitis; the opening of the right ureter was far out on the side wall of the bladder; a thickened interureteral bar led up and into a tunnel which represented the opening ("dragged-out" ureter). Palpation of the kidney on this side produced a powerful tug on this

FIG. 21.

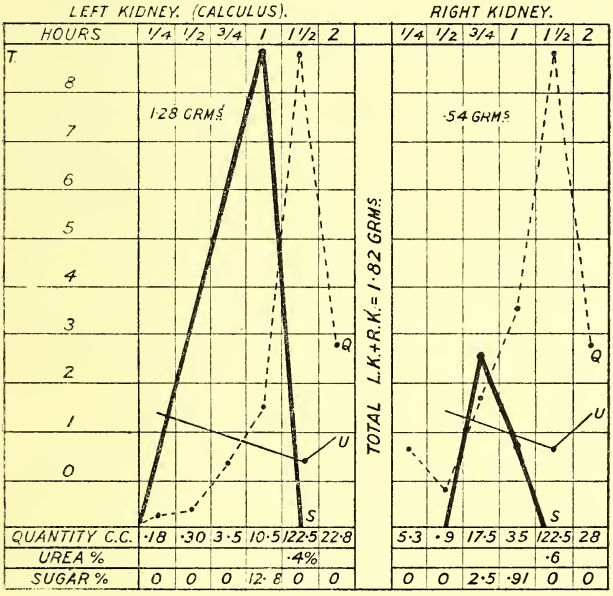


Case of moveable kidney. Elimination of sugar greater on diseased side.

muscular ridge. I catheterised the right ureter, drained the bladder, and injected five milligrammes of phloridzin. No sugar appeared in the urine collected from the right ureter and the urea varied from 0·8 to 1·0 per cent. The urine from the left kidney contained 0·296 gramme of sugar and the urea varied from 2·4 to 2·6 per cent. (Fig. 19). Mr. Freyer cut upon the right kidney and removed a large kidney containing masses of caseous material and a thickened ureter.

Phloridzin failed to produce glycosuria on one side while it appeared in much reduced quantity on the other in two cases, where there was apparently insufficient cause. In one, a case of right-sided moveable kidney, the supposed healthy kidney eliminated no sugar while the moveable kidney produced only 0·037 gramme. In another, a very nervous man with attacks of left-sided renal colic and a history of hæmaturia, the painful kidney eliminated 0·46 gramme of sugar and the supposed healthy kidney none at all.

FIG. 22.



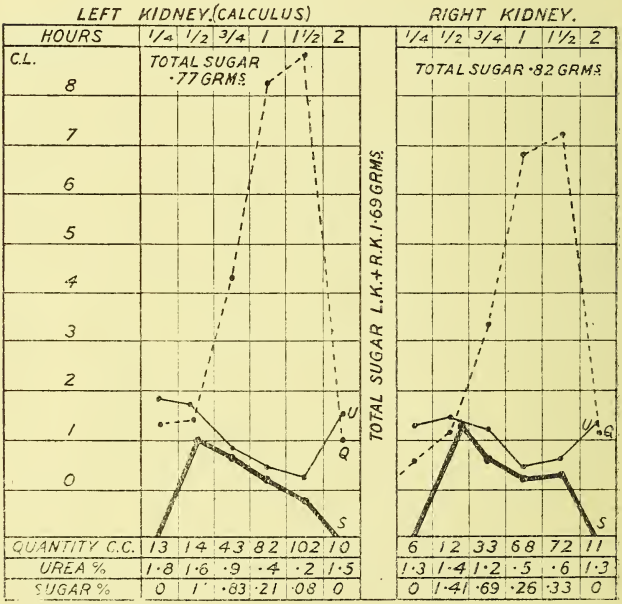
Calculus in left renal pelvis. Normal glycosuria. Percentage of sugar excessive on diseased side.

The quantity of sugar eliminated on the diseased side was diminished while that from the healthy kidney was normal in a case of pyonephrosis containing large masses of calculi (0·395 gramme and 1·623 gramme) (Fig. 20). On the other hand, the elimination on the diseased side in a case of moveable kidney was greater than that on the healthy side (Fig. 21), and in a case of stone in the renal pelvis there was a striking increase in the percentage of sugar in the urine on the diseased side over that present on the healthy side (Fig. 22). In another case of renal pelvic calculus of small

size the elimination of sugar on the two sides was practically equal (Fig. 23).

Where sugar is eliminated at all by a diseased kidney the commencement of the glycosuria is frequently delayed beyond half an hour. It is usual when a diminished quantity of sugar is eliminated by a kidney for the glycosuria to last for a shorter period of time. Frequently it is over in a quarter of an hour, sometimes in half an hour.

FIG. 23.



Calculus of left renal pelvis. Elimination of sugar practically equal on two sides.

Clinical value of the test.—As a means of demonstrating the diseased side the phloridzin test is frequently more delicate than other methods. The fallacies which attend its use have already been noted. It must detract from the value of the test that cases have been observed when a diseased kidney eliminated a full quantity of sugar and a healthy (or supposed healthy) kidney passed none at all. A disadvantage of the phloridzin method is that it is very sensitive to slight changes in the kidneys and an exaggerated idea of

the extent of the disease may be obtained by studying the glycosuria produced. Larger doses than those in use are more accurate, for there is less probability of a total absence of the glycosuria in slight lesions (Albarran). The cases in which these fallacies occur are exceptional and in the majority of cases in which I have used this method the result has proved reliable when tested by other methods or by operation. The short duration of the glycosuria is an undoubted advantage where the comparative work of the kidneys is in question. I have seldom required to prolong the examination beyond two hours in order to complete the phloridzin test. Where the phloridzin test is combined with an artificial polyuria it forms, I believe, a valuable method of estimating the function of each kidney.

Albarran's experimental polyuria test.—Albarran has established two general rules:—1. A diseased kidney has a much more uniform function than a healthy kidney and its function varies less from one moment to another the more its parenchyma is destroyed. 2. When one kidney alone is diseased or is the more diseased of the two, if the urinary function becomes disturbed it modifies its function less than the other, and the difference between the two glands is especially exaggerated by the variations in the function of the healthy kidney. If instead of examining comparatively the total quantity of urine secreted by each kidney during a certain space of time a series of fractions of the same time are compared, the course of the function of each kidney may be studied. Curves may thus be constructed for comparison of the work of the kidneys, and according to Albarran the differences between the two kidneys may be accentuated in making them perform during the examination a supplementary labour, such as the elimination of water or of phloridzin glucose. Albarran estimates the quantity of urine, the point Δ and Δ V, urea per litre and in centigrammes, the sugar per litre and in centigrammes. In the normal state the curves of the two urines follow each other and present similar variations (see Fig. 21). In pathological conditions the differences in the curves of each gland are readily observed. The sound kidney should show a reaction after drinking Evian water (Fig. 20). The curve of the quantity of urine should be elevated at the same time that the Δ is lowered and the urea and chlorides per litre are diminished. These oscillations should be evident and affect several divisions. One may consider satisfactory the elimination, by one kidney in an adult man, of from 1·20 grammes to 1·80 grammes of urea during the two hours of the test. Below 75 centigrammes to one gramme may be regarded as a faulty excretion. The Δ V presents as great variation as the quantity of urea. In a man one may look upon from 12,000 to 17,000 as good, from 8000 to 10,000 as mediocre, and 6000 and below as an impaired excretion.

Fallacies of Methods of Ascertaining the Renal Function.

Throughout these tests there run some fallacies that lie beyond the question of a perfect or imperfect technic. One factor is the partial activity of the kidneys in health. The renal function is not in full action at any one time under ordinary conditions. If proof is wanted of this it is to be found in the fact that if the urines of the two kidneys are collected separately and compared it will be found that one kidney is working more actively than the other, while at another time the kidney, which was less active, is now working with greater energy, yet over a sufficiently long period the work of the two will be approximately equal. The renal output under any ordinary conditions does not therefore correspond to the full potential function of the kidneys and the activity will increase where greater demands are made upon it. What the safety margin of renal tissue may be, apart from hypertrophic changes, it is difficult to say. Certain it is, from the removal of mechanically injured kidneys in the human being where no opportunity for hypertrophy of the second kidney has occurred that the safety margin amounts to half of the total renal tissue.

Mr. Henry Morris records a case [7] which has an important bearing upon this subject. In a woman, aged 20 years, whose right kidney had been removed by another surgeon for tuberculous disease four years previously, he excised a tuberculous nodule involving about one-third of the left kidney. Seven years later this remaining portion of the kidney was explored and a quantity of pus was evacuated. The patient died four and a half months later from acute tuberculosis of the lungs. "Only two-thirds of one kidney existed and this remaining piece was very extensively fibrosed, so that the actual amount of secreting tissue must have been very small indeed." It appears, therefore, that the amount of renal tissue necessary for the secretion of an adequate quantity of urine is less than half the total quantity. The experiments of Dr. J. Rose Bradford [8] on animals have shown that two-thirds of the total kidney tissue may be removed and the animal remain in good health, but if the quantity of kidney tissue be reduced to one-quarter death occurs after an interval. It is this margin of safety that introduces a fallacy into the methods of estimating the renal function. A kidney disease may operate within this and give no sign of its incursions upon the potential renal function until an operation such as nephrectomy reveals the fact that the patient has been living upon the minimum of kidney tissue and even a very slight reduction of this or a

[7] Archives of the Middlesex Hospital, vol. vi., p. 1.
[8] Proceedings of the Royal Society, London, 1892.

temporary interference with its action is sufficient to overturn the balance and to produce suppression of urine.

Although it is apparently beyond the range of practical surgery at the present time to estimate the potential renal activity, yet some approach to it might, I think, be made by the coincident use of diuretic drugs with the artificial means of estimating the renal function.

Further, we cannot foretell how far hypertrophy will compensate for the reduction of kidney tissue. Tuffier [9] has studied this question by experiments on animals and concludes that compensatory hypertrophy only takes place when the kidney is partly or wholly normal. If it is the seat of parenchymatous nephritis the hypertrophy fails. According to this observer the quantity of renal parenchyma necessary for life is equal to about a quarter of the weight of the entire kidney tissue. A portion of kidney tissue equal to this weight suffices to reconstruct (by compensatory hypertrophy) a quantity of parenchyma equal in weight to one entire kidney

Another factor is the difficulty in distinguishing between temporary functional depression and permanent reduction of function. To take an example, the obstruction of an enlarged prostate causes a reduced renal function that is partly temporary and partly permanent, the former being due to existing obstruction and the latter to interstitial changes in the kidney brought about by the obstruction. The removal of the obstruction will in such a case be followed by improvement in the renal function which it is impossible to measure beforehand. Yet upon this improvement the progress of the patient may depend after he has survived the removal of the obstruction.

Again, in the case of kidney disease the function of the second kidney may suffer depression partly from changes in its substance and partly, or perhaps wholly, from the reflex influences passing from its diseased neighbour. The removal of the diseased kidney or the source of irritation in it may be followed by a striking improvement in the function of a healthy or slightly diseased second kidney.

In these lectures I have endeavoured, in however hurried and imperfect a manner, to place before you some of the methods which are now within the reach of the surgeon in attempting to estimate the function of the kidney in surgical diseases of these organs. And at the outset I pointed out the limits which might be set upon the estimation of the renal function. It is no part of this work to suggest that the presence of renal disease should form a barrier to operation upon the lower urinary tract nor to surgical interference in the kidneys. The estimation of the renal function in surgical diseases has for its object the recognition of these

[9] Études Expérimentales sur la Chirurgie du Rein, Paris, 1889.

cases which are hopeless from the permanent inadequacy of the renal function and their exclusion from operation.

In conclusion I would tender to the Council of the College my grateful thanks for the honour which it has conferred upon me in selecting me to deliver these lectures, thus enabling me to participate in the annual festival by which the College commemorates the name of John Hunter.

Printed at The Lancet Office, 423, Strand, W.C.